

upon which diverse chemical compounds can be made. Compounds possessing this chemical scaffold are known in the art to be useful in human or veterinary medicine and in plant protection. This invention also provides for some novel intermediate compounds which possess the phosphorus containing backbone.

Applicants respectfully petition, pursuant to 37 C.F.R. 1.17(a) and 1.136(a), a three-month extension of time, i.e., up to and including August 29, 2000. Enclosed herewith is a check for \$870.00 in payment of the fee thereof. Any deficiency or overpayment in this fee, or any other fee occasioned by this paper or any overpayment in any other fee occasioned by this paper may be charged or credited to Deposit Account No. 50-0320.

Applicants wish to thank the Examiner for acknowledging the claim to priority under 35 U.S.C. 119 (a)-(d) based on U.S. Provisional Application No. 60/061,619, filed October 9, 1997, now expired, and from German Patent Application No. 197 45 628.6, filed October 10, 1997. As discussed below, the appropriate reference to these applications is added by this amendment.

Applicants note that the Examiner made the Restriction Requirement final. Applicants traverse this Requirement for reasons of record, however, in order to advance prosecution of this application, Applicants canceled non-elected claims 10 to 15 and expressly reserve the right to file divisional applications directed to the non-elected subject matter.

Claims 1 to 15 are pending in this application. Claims 10 to 15 stand withdrawn by the Examiner from further consideration, under 37 CFR 1.142(b), as being drawn to a non-elected invention. This amendment cancels claims 10 to 15. Claim 1 is also cancelled by this amendment and new claim 16 has been added to define more distinctly the subject matter which the Applicants regard as their invention. Support for new claim 16 is found in the specification

and the claims as originally filed. No new matter is added by this amendment and these amendments is made in order to advance prosecution of this application without any prejudice, admission, surrender of subject matter, or any intention of creating any estoppel as to equivalents.

Claims 1 to 9 were objected to in the Office Action because of the alleged improper use of idiomatic English and due to grammatical errors. (Office Action, page 3, nos. 7 to 8).

This amendment cancels claim 1 in favor of new claim 16. Applicants rewrote claim 1 in order to avoid the grammatical errors found in the original claims. With regard to process claims 2 to 9, these dependent claims include listings of specific substitutions for the various radicals of new claim 16. No additional grammatical errors were found in these claims. If the Examiner still finds these claims objectionable, Applicants respectfully request that she identify the objected to phrases.

Accordingly, Applicants respectfully request withdrawal of this claim objection to claims 1 to 9.

The disclosure was objected to because the specification did not include a reference to the prior applications from which this application claims priority under 35 U.S.C. §§ 119(e) or 120. (Office Action, page 4, nos. 9 to 11).

By this amendment, the appropriate heading for the RELATED APPLICATIONS section, as well as a brief description identifying that the application claims priority from U.S. Provisional Application No. 60/061,619, filed October 9, 1997, now expired, and from German Patent Application No. 197 45 628.6, filed October 10, 1997, is inserted into the specification.

Applicants respectfully request that the objection to the specification be withdrawn.

Claim 1 was rejected under 35 U.S.C. § 101 because the claimed recitation of use allegedly results in a claim that is not a proper process claim under 35 U.S.C. § 101. (Office Action, page 4, nos. 12 to 13).

By this amendment, Applicants cancelled claim 1 in favor of new claim 16. Claim 16 is written as a proper process claim fulfilling the requirements of 35 U.S.C. § 101, and incorporates the helpful suggestion of the Examiner, namely, claim 16 recites “a process for preparing chemical compounds of formula (I).” The phrase “using intermediates which are linked to a resin polymer,” which was interpreted as a “method of using” is not included in new claim 16.

Applicants therefore respectfully request that the rejection of claim 1 under 35 U.S.C. § 101 be withdrawn by the Examiner.

Claims 1 to 14 were rejected in the Office Action under 35 U.S.C. § 112, second paragraph, as being vague and indefinite. In view of the foregoing, reconsideration and withdrawal of this rejection is respectfully requested.

The invention relates to the technical field of combinatorial chemistry, specifically solid-phase based chemical processing (the specification refer to the literature, citing such references as Fruchtel et al.) This type of chemistry developed for preparing large amounts of screening compounds in a very efficient and systematic way. The utility of the invention is a technical utility and of commercial interest for all companies performing research in the field of biologically active compounds or compounds which have specific useful physical properties.

The utility is thus similar to the utility of a novel process for preparing hitherto known or unknown chemical compound having interesting or potentially interesting properties.

Some terminology as used in the application is typical and well known to the person skilled in the art of combinatorial chemistry. These rejections are allegedly due to particular claims language which was described in the Office Action as vague or indefinite. However, Applicants have structured the claims with the degree of precision necessary for the subject matter claimed and the claims are clear and understandable to one skilled in the art when read in light of the specification.

A claim is definite if the scope of the subject matter embraced by a claim is clear and if the applicant has not otherwise indicated that he intends the claims to be of a different scope. In re Borkowski, 164 USPQ 642 (CCPA 1970). The “distinctly claim” requirement of 35 USC § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in light of the completely patent document. Standard Oil Co. v. American Cyanamid Co., 227 USPQ 293 (Fed. Cir. 1985). The test of definiteness is whether one skilled in the art would understand the scope of the claim when read in light of the specification. Morton Int. Inc. v. Cardinal Chem. Co., 28 USPQ2d 1190 (Fed. Cir. 1993). The degree of precision necessary is a function of the subject matter claimed. Hybritech Inc. v. Monoclonal Antibodies, Inc., 231 USPQ 81 (Fed. Cir. 1986).

The purpose behind the combinatorial process is the creation of chemical libraries in an efficient way. An important feature of the inventive process is not the specific modification reactions. Rather, it is the specificity of the resin-linker adduct and its broad practical use. As mentioned in the specification, the process is not limited to specific modification reactions or specific reaction conditions. The modification reactions are carried out

under normal conditions known in the art for non-resin-bound reaction. Therefore, the definition of the type of modification reactions and substituents are not necessary for one skilled in the art to practice the invention as claimed.

For the reasons that follow, Applicants respectfully urge that the terms used in the claims convey a clear meaning to a practitioner in this art, when the terms are read in the context of the rest of the claim and in light of the specification. Moreover, Applicants urge that this language is precise in view of the nature of the claimed subject matter. Accordingly, these terms are precise and therefore not indefinite or vague and clearly described in the specification.

Claims 1 to 9 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being incomplete due to the omission of essential structural cooperative relationships of the elements. (Office Action, page 5, nos. 14 to 15).

Claim 1 is cancelled by this amendment in favor of new claim 16. Applicants respectfully assert that new claim 16, and thereby claims 2 to 9 which are dependent on new claim 16, is complete and includes the necessary structural cooperative relationships of the elements essential for one skilled in the art to practice the invention and fulfills the requirements of 35 U.S.C. § 112, second paragraph.

As discussed above, the invention relates to the field of combinatorial chemistry. This type of chemistry is utilized for preparing large amounts of screening compounds in a very efficient and systematic way.

Some terminology as used in the application is common and well known to one skilled in the art of combinatorial chemistry. For instance, the term "linker" is such a common term. It is defined as a compound or a structural moiety in a chemical compound, wherein the functional group or groups of the linker are able to react with a functional group of another

compound to form a bridge which later can be removed and whereby the compound bound by the linker is cleaved off. Depending on the specific linker, the compound can be split off containing the functional group as originally added or in a modified form.

For this reason, the definition of "Y" and "linker" in the definition of formula (I) is not arbitrary or vague. The compounds of formula (I) are structurally defined in more detail by one skilled in the art defining the structurally moieties of the formula  $-R^1-P(=O)O-R^3)-R^2$  and the group "Y", which depends on the specific linker chosen for the particular process. This is similar to functional or generic definitions such as "leaving group", "acceptor group", "nucleophilic group", "electrophilic group", "acidic group", "basic group", "unsaturated group", which are used in defining process steps to express a functional property of a molecule or functional group.

Within the context of "linker" molecules of functional groups, the definition of linker and the respective functional groups, such as Y in formula (I) or Z in formula (II), are not only clear from the functional properties but are also clear from their basic structural features.

With respect to the inventive process claimed in new claim 16, details of the linkers *per se* are not relevant. The linkers used in the process as described in the specification are for known linkers, however, it should be noted that the process is not limited to the use of known linkers and would work with novel linkers as well. The invention rests on the finding that resin-bound synthesis is valuable for the preparation of compounds where the group of the formula  $-P(=O)(O-R^3)-R^2$  has to be introduced onto an aromatic or heterocyclic radical, such as a group of the formula  $-R^1$ , or an aromatic or heterocyclic precursor thereof. A further object of the invention is to be able to use the process to find compounds having said phosphorus-containing functional groups that are suitable for resin-bound modification of the radicals on said group.

Therefore, Applicants assert that the processes as claimed in claims 2 to 9 and 16 are complete, describe the metes and bounds of the invention to one skilled in the art, and fulfill the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request that the rejection of these claims be reconsidered and withdrawn.

Claims 1 to 14 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite due to an insufficient antecedent basis for a number of terms in the claims. In particular, use of “the” without proper antecedent basis for the so modified claim term was objected to. (Office Action, page 6, nos. 16 and 17).

Claim 1 is cancelled by this amendment in favor of new claim 16. The preamble includes the changes, as helpfully suggested by the Examiner in the Office Action, and the claim terms each have a proper antecedent basis in the claim. With respect to claims 2 to 9, which are dependent on new claim 16, since they recite specific substitutions for the various substituent groups, the proper antecedent for these claim terms rests in new claim 16.

Therefore, Applicants respectfully request that this rejection of the claims under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

Claim 1 was rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite and vague, and/or for having improper antecedent basis for a number of reasons, delineated [A] to [H]. (Office Action, page 7 to 10, no. 18). The bases for these rejections, with respect to the claim terms in question, shall be individually addressed below.

With respect to [A], terms used to describe substituents  $R^1$ ,  $R^2$ ,  $R^3$ , and Y were objected to. The antecedent basis objection relating to Y, rejection [3], has been addressed in new claim 16, wherein the definition of Y has been corrected.

Applicants assert that the definition of  $R^1$  is a broad definition but not a vague definition. As explained above, the important property of the radical  $R^1$  is that the radical is an aromatic or heteroaromatic radical. The substitutions on the aromatic or heteroaromatic radicals are based on independent selections made by one skilled in the art in practicing the claimed invention. Therefore, rejection [1] based on the definition of  $R^1$  should be reconsidered and withdrawn.

Radicals  $R^2$  and  $R^3$  are broadly defined as organic radicals. There is a difference, however, in the specific atom by which these radicals are bound to the phosphorus or oxygen atom in formula (I). While  $R^2$  may be bound to the phosphorus atom “by” (replacing via) a carbon atom or a heteroatom, the radical  $R^3$  must be attached to the oxygen atom “with” (replacing via) a carbon atom. It would be clear to one skilled in the art that the heteroatoms are a part of the radical. (See specification, page 9, lines 5 and 6).

With respect to [B], the terms used to describe resin-polymer, as in rejection [4], do have a proper antecedent basis in new claim 16.

Further, with regard to the definition of Z, rejection [5], Z relates to the functional group of a linker which is transformed to Y by cleavage of compound (I) from the resin polymer in the last step of the process. The structure and function of Z is described to one skilled in the art in the specification on pages 13 to 14, bridging paragraph.

With regard to the definition of  $E^1$ , rejection [6],  $E^1$  is defined functionally because the specific definition of  $E^1$  is an independent selection made by one skilled in practicing the invention. The relationship between  $E^1$  or  $(E^1)'$  and  $R^1$  is one of precursor and final product. The combinatorial process allows for broad variation of the moieties  $E^1$  and  $R^1$ . The teaching of the invention is that modifications can be made on the solid-phase bound



intermediates, and after the modifications, the final product can be cleaved from the resin. A claim limitation for very specific modifications would be arbitrary, and would not be required to convey the full scope of the claimed invention to one skilled in the art.

With regard to the definition of S, rejection [7], an important feature of the combinatorial process of the present invention is the palladium-catalyzed substitution (analogous to the Heck-reaction) of the group S<sup>1</sup> to form the phosphorus containing functional group at the heteroaromatic system. The objection to the definition of S<sup>1</sup> is also not proper. The Heck-reaction is well known and described in the specification on page 21, line 20 to page 22, line 25. At page 22, lines 6 to 14, the preferred definition for S<sup>1</sup> is also mentioned. Therefore, the term is used in a similar manner as common terms such as "esterification", "Michael-addition", "Diels-Alder-cycloaddition", and should be acceptable. Hence, the terms have a definite meaning to one skilled in the art when read in light of the specification.

With regard to the definition of n, rejection [8], n is the number of the functional groups n in the resin-linker adduct of formula (II). The antecedent basis for n is in formula (II) and based on the definition of resin polymer, whereby n is also selected by one skilled in the art practicing the invention.

The rejection in [9] is similar to the objections to step (a) above. Applicants assert that various derivatization reactions are possible. The specific definition is an independent selection made by one skilled in the art in practicing the invention. The process is not limited to specific derivatization reactions. Therefore, the terms have antecedent basis in the formulae given in step (a) of new claim 16.

With respect to the definition of [A], rejection [10] is similar to the objections to step (a) above. Applicants assert that various derivatization reactions are possible. The specific

definition of an organic radical is an independent selection made by one skilled in the art in practicing the claimed invention. The process is not limited to specific derivatization reactions. Therefore, the terms have antecedent basis in the formulae given in step (a) in new claim 16.

With respect to the definition of A\*, rejection [11] is similar to the objections to step (a) above. Applicants assert that various derivatization reactions are possible. The specific definition of an organic radical is an independent selection made by one skilled in the art in practicing the claimed invention. The process is not limited to specific derivatization reactions. Therefore, the terms have antecedent basis in the formulae given in step (a) in new claim 16.

With respect to rejection [12], a reaction analogous to the Heck-reaction is defined by indicating the reactant of formula (III), the starting compound of formula (II), the functional group S<sup>1</sup> where the reaction is to take place, and the product of formula (IV). Applicants assert that it is clear from this definition, and the knowledge of one skilled in the art, that the group S<sup>1</sup> is substituted with the group of the formula -P(H)(=O)-O-A<sup>1</sup>.

With respect to the derivatizing reaction of step (b), rejection [13] is similar to the objections to step (a) above. Applicants assert that various derivatization reactions are possible. The specific definition is an independent selection made by one skilled in the art practicing the claimed invention. The process is not limited to specific derivatization reactions. Therefore, the terms have antecedent basis in the formulae given in step (b) of new claim 16.

With respect to the claim terms of rejection [14] is similar to the objections to step (a) above. Applicants assert that various derivatization reactions are possible. The specific definition is an independent selection made by one skilled in the art practicing the claimed invention. The process is not limited to specific derivatization reactions. Therefore, the terms have antecedent basis in the formulae given in step (b) of new claim 16.

With respect to the claim terms of step (c), rejections [15] and [16], the term "if appropriate" clearly refers to the reactions where  $A^1$  is hydrogen versus where  $A^1$  is different from hydrogen. In the latter case, a hydrolization reaction is possible. In the former, the hydrolization product is the starting material and hydrolization is not appropriate. Additionally, the hydrolization product may not be the desired product in view of the product of formula (I) desired by one skilled in the art. A comparison of the phosphorus containing groups in formula (I) with formula (V) or (V)' would make it clear to one skilled in the art, whether the process step would be appropriate or not. In addition, the compounds (IV) and (IV)' have antecedent basis in process steps (a) and (b), respectively. The phrase "suitable for the resin bound synthesis" has not been included in new claim 16, as the term was superfluous in original claim 1.

With respect to the claim terms of step (d), rejections [17] and [18], the phosphorus-containing groups in compounds (VI) to (VI)' may not be the desired phosphorus-containing groups in view of the product of formula (I) desired by one skilled in the art. A comparison of the phosphorus containing groups in formula (I) would make it clear to one skilled in the art whether the process step would be appropriate or not. In addition, the compounds (V) to (VI)' are defined in process steps (c) and (d), respectively.

With respect to the claim terms of step (e), rejections [19], [20], and [21], the phosphorus-containing groups in compounds (VII) to (VIII)' may not be the desired phosphorus-containing groups in view of the product of formula (I) desired by one skilled in the art. A comparison of the phosphorus containing groups in formula (1) would make it clear to one skilled in the art whether the process step would be appropriate or not. In addition, the phosphonous acid and phosphonous ester groups are shown in the chemical formulae of the compounds referred to by numbers (IV) to (VI)'. Additionally, in process step (e), the radical  $R^2$

or  $E^2$  is introduced in the intermediate compound by reaction with the respective precursor compound of formulae (IV) to (VI)'. Particular reaction variants are discussed in the specification on page 23, line 22 to page 24, line 19 of the specification. Additionally,  $R^2$  is defined in formula (I).

With respect to the claim terms of step (f), rejections [22] and [23], the other terms objected to are defined in the previous process steps and have an antecedent basis in new claim 16. The phrase "resin-bound" was superfluous in original claim 1 and is not included in new claim 16. Additionally, it would be apparent to one skilled in the art from the formulas that the compound is still resin-bound.

With respect to the claim terms of step (g), rejection [24], if the Examiner believes that there are still claim terms without proper antecedent basis, Applicants respectfully request that the Examiner particularly point them out. All of the terms objected to have antecedent basis in the definition of previous process steps or in formula (I) in new claim 16.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of all of the rejections of the claims based on 35 U.S.C. § 112, second paragraph, because the terms in the claims are not vague nor indefinite and clearly define the subject matter of the present invention based on the degree of precision necessary for the subject matter claimed.

Claim 2, 3 and 4 was rejected under 35 U.S.C. § 112, second paragraph, for allegedly being vague and indefinite because of the definition of  $R^1$ ,  $R^2$ , and  $R^3$ . (Office Action, pages 10 to 11, no. 19, 20, and 21).

Applicants respectfully assert that the terms in claims 2, 3, and 4 are not vague and indefinite and that claims 2, 3, and 4 fulfill the requirements of 35 U.S.C. § 112, second paragraph.

With respect to the use of the term “substituted” in claims 2, 3 and 4, Applicants assert that this term is definite when read in light of the specification and based on the knowledge of one skilled in the art. Various substituents are generically defined in the specification on pages 8 to 13, with specific examples provided on page 10, line 10 to page 11, line 2. Moreover, the term “substituted” is well known to those skilled in the chemical art. Hence, one skilled in the art would know which groups are contemplated when the term “substituted” is read in light of the specification.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of all of the rejections of claims 2, 3, and 4 based on 35 U.S.C. § 112, second paragraph, because the terms in the claims are not vague nor indefinite and clearly define the subject matter of the present invention based on the degree of precision necessary for the subject matter claimed.

Claim 8 was rejected under 35 U.S.C. § 112, second paragraph for allegedly being vague and indefinite for the recitation of term “electrophile” associated with variable A<sup>4</sup>. (Office Action, page 12, no. 22).

Applicants respectfully assert that the terms in claim 8 are not vague and indefinite when read in light of the specification, together with the knowledge and level of skill of a practitioner in this art. Hence, Applicants assert that these terms are clear and definite.

The term “electrophile” is a commonly accepted term of art and would be readily understood by one skilled in the art. The inventive process defines the starting materials, as well

as the products of the reaction with an electrophile. The specification provides examples of electrophilic reactants and describes in detail the various reactions where these electrophiles are used. (See specification, pages 26 to 28). Hence, the term “electrophile” would have a clear and definite meaning to one skilled in the art.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of all of the rejections of claim 8 based on 35 U.S.C. § 112, second paragraph, because the terms in the claims are not vague nor indefinite and clearly define the subject matter of the present invention based on the degree of precision necessary for the subject matter claimed

Claims 1 to 9 were rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Schwabacher et al (“Schwabacher”)(Synthesis, 1992, pp. 1255 – 1260) in combination with Boyd et al. (“Boyd”)(Tetrahedron Letters, Vol. 37, No. 10, 1996, pp. 1647 – 1650).

As neither of these publications taken alone, or in any fair combination, teach or suggest the inventive process, Applicants urge that the rejection does not establish a *prima facie* case of obviousness. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

The Office Action states on page 14 that Schwabacher does not teach:

- (1) the formation of phosphinic acid compounds and their derivatives on a solid support resin;
- (2) an organic starting material intermediate being first anchored to a solid support resin; nor
- (3) the addition of the phosphorus containing intermediate leading to the formation of phosphinic acids and derivatives.

The Office Action alleges that Boyd teaches the use of a resin for the multiple phase synthesis of phosphinic acid containing products on a resin. From this, the Office Action alleges that a person of ordinary skill in the art would have been motivated to develop a method for the

preparation of substituted phosphinic acids and its derivatives and that one skilled in the art would have had a reasonable expectation of success based on the teachings of Schwabacher, in combination with Boyd.

Applicants respectfully maintain that the claims are not obvious based on the combined teachings of Schwabacher and Boyd, and further that the references fail to constitute a *prima facie* case of obviousness, because there is no motivation or suggestion in either of the references to utilize the solid phase reactions and processes claimed in the present application.

Therefore, Applicants respectfully request the withdrawal of the rejection of the claims under 35 U.S.C. § 103(a) based on Schwabacher, in combination with Boyd, because Schwabacher does not teach the claimed invention for the reasons cited in the Office Action, and Boyd does not correct the deficiencies of the Schwabacher reference as Boyd does not teach solid phase synthesis for compounds where the phosphorus atom is bound to a heteraryl or aryl moiety. There is no motivation to combine these references because Boyd teaches a different reaction and does not indicate that the processes disclosed therein are equivalent to the solution reactions taught by Schwabacher. Further, this combination does not suggest the superior yields obtained by the inventive process. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Schwabacher discloses the preparation of methyl esters of monoarylphosphinic acids which involves palladium catalyzed coupling of aryl iodides with methyl phosphinates in the presence of tertiary amines or propylene oxides. Both symmetrically and unsymmetrically substituted diarylphosphinate are disclosed. The table on p. 1255 of Schwabacher summarizes the yields of the reactions based on the teachings of Schwabacher. These yields range from 23% to 80%.

In contrast to the disclosure in Schwabacher, the present invention teaches a combinatorial process using solid phase bound intermediates. Surprisingly, the palladium catalyzed Heck reaction process of the present invention works well with the solid phase bound starting materials. It would not have been expected that the reaction would work at all with the resin bound material. In principle, many side-reactions may occur on the resin. The solid phase reaction (for example, the Heck reaction and subsequent derivatization reactions) work even better, i.e. result in better yields, when compared with similar reactions in solution. (See Specification, page 8, lines 3 to 14). The yields reported by Schwabacher for the step of the Heck reaction recorded in the table on page 1255 are 23 to 80% of theory. In contrast, the processes of the present invention produce final products in higher yields, with yields in excess of 90% after cleavage of the final product from the resin.

These high yields are seen for other examples in the specification as well. Example 2 (Specification, page 37, line 16 to page 38, line 4) for the palladium-catalyzed reaction and Example 3 (Specification, page 38, lines 7 to 29) for the modification with an aldehyde and subsequent cleavage of the final product provide an example with a yield of 92%. Similarly, the combination of Example 2 with the reaction of Example 4 (Specification, page 39, lines 1 to 20) provide a further example with a combined yield of 94.6%.

These surprisingly good yields, together with the broad variability allowed for the phosphorus-containing group and the substituents thereon in practicing the invention, demonstrate the non-obviousness of the invention over the prior art cited, as these processes would not have been expected to proceed so efficiently based on the prior art cited.

Further, there is no suggestion or motivation in Schwabacher to utilize the solid phase support taught by Boyd, or any other solid phase support resin, for the reactions taught in



Schwabacher. In fact, Schwabacher would lead one skilled in the art away from combining the Schwabacher with the Boyd references. Schwabacher states on page 1257, column 1, third paragraph, "Attempts to use trimethylsilyl and tributylstannyl esters of hypophosphorus acid led to only trace quantities of the desired phosphinates. Water scavengers such as *bis*(trimethylsilyl)acetamide or molecular sieves also failed to improve the yields in reactions of methyl phosphinate." Boyd teaches the use of *bis*(trimethylsilyl) phosphinate in the reaction forming 1-aminophosphinic acid. Therefore, one skilled in the art would not have been motivated, nor would one skilled in the art have a reasonable expectation of success, based on Schwabacher in combination with Boyd.

Further, there is no suggestion or motivation in Boyd for one skilled in the art to combine the teachings in Boyd with Schwabacher and practice the invention of this application. Boyd et al does not teach the solid phase synthesis of compounds whereby the phosphorus atom is bound to a heteroaryl or aryl moiety as in the present invention.

Boyd teaches the synthesis of 1-aminophosphinic acids, whereby 9-amino-xanthen-3-yloxymethyl polystyrene is reacted with an aldehyde. A phosphate group is added to the substituent added on the amino group through the use of *bis*(trimethylsilyl)phosphinate. The final product, 1-aminophosphinic acid, is produced by cleavage of the amino group from the xanthene-3-yloxymethyl polystyrene, without further substitution on the phosphorus atom. Boyd does not teach or suggest any other substitution on the phosphorus atom, nor is there any suggestion to bind a phosphorus atom directly to the solid support and provide further substitution or derivatization on the phosphorus atom. Therefore, one skilled in the art would not be motivated to combine the teachings of Boyd with the teachings of Schwabacher, because Schwabacher teaches chemical substitution directly on the phosphorus atom and Boyd does not.

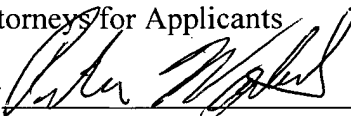
Thus, in view of the foregoing, reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

In view of these amendments and remarks, it is respectfully requested that this application is now in condition for allowance. Reconsideration of this application, consideration of new claim 16 and prompt issuance of a Notice of Allowance, with claims 2 to 9, and 16, are earnestly solicited. If there are any minor issues which remain an impediment to allowance, the Examiner is respectfully requested to contact the undersigned by telephone.

Respectfully submitted,

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